not been successful. It might be quite important, therefore, to make a presumptive diagnosis on the basis of clinical and laboratory findings of severe acidosis without ketosis and elevated phosphorus, and to begin treatment accordingly without immediate confirmation of elevated lactate levels, unless facilities for determining lactate content of the blood are at hand.

Daughaday and coworkers[2] have reported adequately documented cases of nonketotic acidosis in diabetic patients. The patients were not taking phenformin. Generally the response in those cases to therapy with sodium bicarbonate was rapid and good. The variability in the elevation of lactate and the clinical correlation with the degree of acidosis in coma has been apparent to many investigators.[3] The patient in the present case, who had a history of hypertension, had clinical symptoms of severe acidosis with rapid progression and apparent deterioration associated with hypotension. It was because of the clinical condition and a reduction of pH to 6.83 that the vigorous therapy was undertaken. Retrospectively one wonders if improvement might not have been equally good with large amounts of bicarbonate along with other supportive measures, without methylene blue. However, from review of the literature it is apparent that in cases in which there is derangement of the acid base balance and an associated clinical deterioration or considerably altered status sensorium, the patient usually dies. Moreover, in the present case, on suspicion that there might be a pharmacological anoxic derangement of the normal metabolic or oxidative pathways, bicarbonate was given early to correct the acidosis; and then methylene blue was added to provide an alternate oxidative system as had been outlined by Tranquada and coworkers.[5]

Perhaps the favorable outcome in the present case was owing to the early beginning of vigorous bicarbonate therapy, although Tranquada[6] and Bernier[1] reported early treatment without success. The arterial pH of 6.83 in the present case was among the lowest reported in similar cases, the lowest among cases in which there was so severe a clinical deterioration and the patient lived.

GENERIC AND TRADE NAMES OF DRUGS

Phenformin—*DBI.*
Hydrochlorothiazide—*Hydrodiuril.*
Reserpine—*Serpasil.*
Meclizine dihydrochloride and nicotinic acid—*Antivert.*
Trihexyphenidyl—*Artane.*
Methentermine—*Wyamine.*

REFERENCES

1. Bernier, G. M., Miller, M., and Springate, C. S.: Lactic acidosis and phenformin hydrochloride, J.A.M.A., 184:43-46, 1963.

2. Daughaday, W. H., Lipicky, R. J., and Raskinski, D. C.: Lactic acidosis as a cause of nonketotic acidosis in diabetic patients, New Engl. J. Med., 267:1010-1014, 1962.

3. Huckabee, W. E.: Lactic acidosis, Amer. J. Med., 30:840-848, 1961.

4. Tranquada, R. E.: Lactic acidosis, Calif. Med., 101: 450-461, 1964.

5. Tranquada, R. E., Bernstein, S., and Grant, W. J.: Intravenous methylene blue in the therapy of lactic acidosis, Arch. Int. Med., 114:13-25, 1964.

6. Tranquada, R. E., Bernstein, S., and Martin, H. E.: Irreversible lactic acidosis associated with phenformin therapy, J.A.M.A., 184:37-42, 1963.

Disseminated Tuberculosis Of Bone

EDWIN S. WILSON, JR., CAPTAIN, MC, USA AND EDWARD G. WHITING, JR., CAPTAIN, MC, USA, *San Francisco*

DISSEMINATED BONE tuberculosis is not often reported. O'Malley and coworkers[13] reviewed the world literature and noted that although over 500 cases had been reported, only 60 had been carefully documented by strict pathologic and bacteriologic criteria. Reviewing 36,372 unselected admissions for tuberculosis, McTammany and coworkers[12] reported that osteoarticular tuberculosis was present in 3.8 per cent of patients, and that only 4.6 per cent of this latter group presented with multiple lesions of the skeletal system. Although statistically unsubstantiated at present, there appears to be a trend toward a decreasing incidence of skeletal tuberculosis, reflecting both the control of bovine tuberculosis in the United States and the development of effective anti-tuberculous agents.[6,11,12]

From Letterman General Hospital, San Francisco.

Submitted 7 June 1966.

This material has been reviewed by the Office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

Reprint requests to: Radiology Department, Letterman General Hospital, San Francisco 94129 (Captain Edwin S. Wilson, Jr.).

In 1920 Jungling described a group of patients with cyst-like lesions of the small bones of the hands and feet and negative tuberculin skin tests. He called this disease osteitis tuberculosa multiplex cystica, but eight years later renamed the entity osteitis tuberculosa multiplex cystoides to emphasize the pseudo-cystic nature of the lesions. Ellis[4] in 1939 suggested that the cases reported by Jungling were actually examples of osseous sarcoidosis, and this apparent inconsistency generated much confusion in the literature concerning terminology and roentgenographic manisfestations of skeletal tuberculosis. Alexander and Mansuy[1] in 1950 reported a case of skeletal tuberculosis with multiple bone involvement, and coined the term disseminated bone tuberculosis to describe those cases of multiple bone tuberculosis in adults, with or without a cystic appearance of the lesions roentgenographically. Two years later Komins[9] elaborated on the subject and suggested that those tuberculous lesions of a cystic nature in children be called multiple pseudo-cystic tuberculosis of bone, and that the term disseminated bone tuberculosis be reserved for adults with multiple lesions, as originally proposed by Alexander and Mansuy. The lesions of sarcoidosis were designated as osteitis multiplex cystoides sarcoidosa.

The purpose of the present report is to present a patient with disseminated bone tuberculosis in whom neurologic deficit developed in all four extremities during the period in hospital, but who responded favorably to prompt medical and surgical therapy.

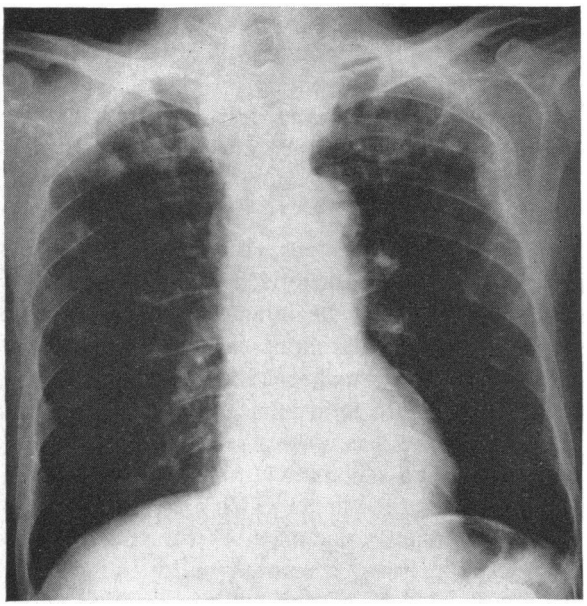

Figure 1.—The x-ray film on admission demonstrating bilateral pulmonary densities and a destructive process evident in the left fourth rib.

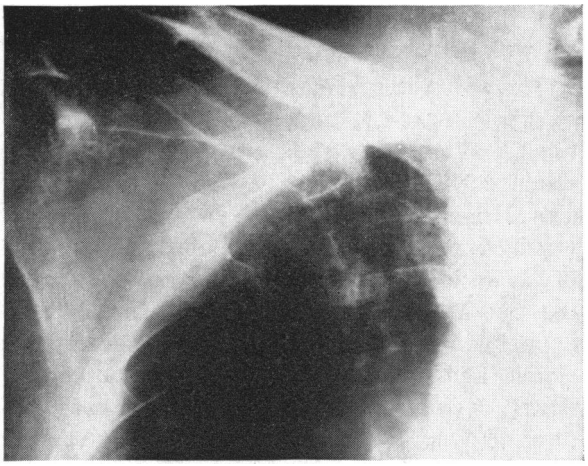

Figure 2.—Bone detail film demonstrating a destructive focus in the right second rib. Similar lesions were noted in the left fourth and twelfth ribs and the right eleventh rib.

Report of a Case

The patient, a 62-year-old Filipino who had entered the United States from the Philippine Islands in May of 1964, was well until, in December of that year, intermittent interscapular pain developed. The pain was aggravated by motion. He was seen at Letterman General Hospital on 25 June 1965, and an x-ray film of the chest showed bilateral pulmonary densities and multiple lytic rib lesions. Inquiry elicited no family history or history of exposure to tuberculosis, and the physical examination was within normal limits with the exception of minimal tenderness over the interscapular region.

X-ray studies of bones showed destruction of the sixth cervical vertebra, probable involvement of the fifth cervical vertebra, and involvement of the disc between the fifth and sixth cervical vertebrae.

On 4 July 1965 the patient had a negative reaction to purified protein derivative (PPD) No. 1. However, six days later there was positive reaction to the intermediate strength PPD intradermally. Numerous septum cultures were negative for acid-fast bacilli. On 12 July an excisional biopsy of the lesion in the left fourth rib showed caseating granuloma as well as numerous acid-fast bacilli within the specimen. Subsequent cultures of material from the rib lesion yielded acid-fast bacilli that

were morphologically and histochemically consistent with mycobacterium tuberculosis.

Therapy with isoniazid, para-amino salicylic ascorbate (PAS-C), and streptomycin was instituted, and a cervical collar was utilized to prevent spinal cord compression in view of the cervical spine lesion. Despite these measures, transient weakness of his right arm developed. At that time it was decided that spinal fusion would be carried out but before it could be done, paresis of all extremities developed, together with bilateral ankle clonus and Babinski reflexes, and bladder and bowel dysfunction. Skeletal traction was instituted and on 13 September fusion of the fourth to seventh cervical vertebrae was performed. The patient progressed satisfactorily, and on 4 October was ambulatory about the hospital. On 14 October he was sufficiently well to be discharged from the hospital with prescriptions of isodiazid, PAS-C and pyridoxine, and up to the time of this report he remained well.

Clinical Findings

Skeletal tuberculosis is invariably due to hematogenous dissemination of the bacilli from primary sites elsewhere within the body. Children and young adults appear to be particularly susceptible to skeletal involvement and in the colored races there is a higher incidence of multiple bone involvement, suggesting increased susceptibility to hematogenous spread of the infectious process.[7,9] In nearly all cases there are demonstrable pulmonary lesions, although cases have been reported without apparent lung involvement.[1,6,8,10,13] It is in these latter instances that a diligent search should be made for other visceral sites of the primary infection, such as the genitourinary tract.

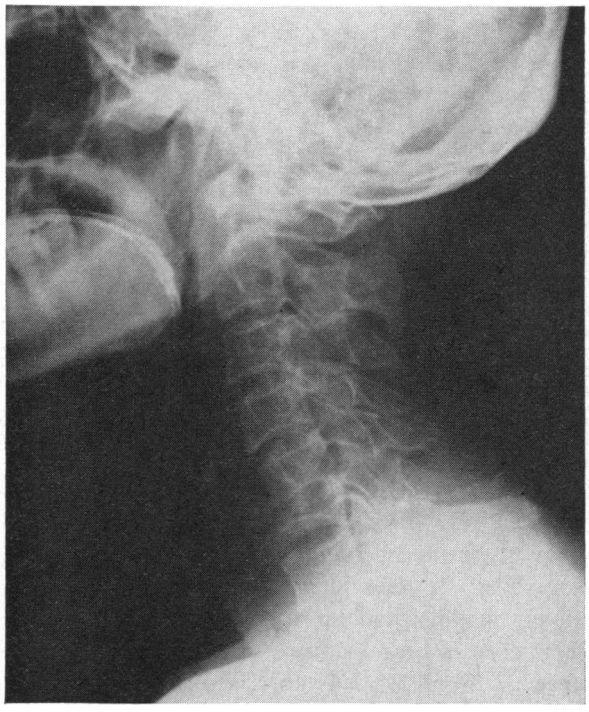

Figure 3.—X-ray film of lateral cervical spine demonstrating the destructive process of the sixth cervical vertebra as well as apparent involvement of a portion of the fifth vertebra and the disc between the fifth and sixth.

Patients with disseminated bone tuberculosis may present with pain, swelling, fever, lymphadenopathy, draining sinuses and neurologic signs secondary to cord compression. In the latter instance, the prognosis is grave. Bosworth and coworkers[3] reviewed a series of 122 patients with paraplegia secondary to skeletal tuberculosis, and noted an overall mortality of 56.5 per cent. Of further prognostic significance was the fact that the mortality rate among patients with complete paraplegia was 69 per cent, whereas only four per cent of the patients with paresis died. In this group of patients the heralding sign of the need for surgical intervention was the development of ankle clonus, as further neurologic decompensation rapidly followed.

Roentgenographic Findings

In adults with disseminated bone tuberculosis the lesions usually involve the bones of the axial skeleton, the most common site being the vertebrae of the thoracic spine.[5,12,13] The flat bones of the pelvis and ribs and the proximal tubular bones are less commonly affected, and there is rarely involvement of more than four sites in adults.

The individual lesions of disseminated bone tuberculosis are characterized by the presence of lytic areas, usually beginning in the cancellous portion when tubular bones are involved, with a minimum of periosteal reaction. With some of the smaller and more indolent lesions, a rim of sclerosis about the lesion may rarely be visualized.[9] More advanced lesions may produce cortical erosion, and it is these areas which may appear cystic or multilocular. Concurrently with the cortical destructive process, a smooth periosteal reaction may occur which may give the impression of an expansile destructive process within the bone. Sequestra are rare. In the spine, involvement of the

intervertebral disk is characteristic. Soft tissue reaction about the lesion may be evident, and this is especially noteworthy with rib lesions, where the extra-pleural density is contrasted against the air-filled lungs, and also with para-spinous masses produced with vertebral lesions. Healing is characterized by disappearance of the destructive foci, and by gradual restitution of the normal trabecular pattern of bone.

Differential Diagnosis

To be considered in differential diagnosis in cases of multiple destructive lesions of bone, in addition to disseminated bone tuberculosis, are multiple myeloma, metastatic malignant disease, the reticuloendothelioses, including eosinophilic granuloma, the lesions of hyperparathyroidism and osteomyelitis of other than tuberculous origin, such as coccidioidomycosis and other fungal diseases. The presence of pulmonary lesions may provide a useful clue to the diagnosis; however, the ultimate diagnosis rests with histologic demonstration of the caseating granuloma and identification of the organism with appropriate bacteriologic and histochemical techniques.

Treatment

Therapy of this disease turns upon adequate administration of chemotherapeutic agents and such surgical procedures as may be indicated by the scope of the disease. Although various regimens of therapy are advocated, the general consensus is that a minimum of two agents is indicated, and that treatment should be continued for at least 24 months, and longer if indicated by the course of the disease.[2,5] Hodgson and Stock[5] proposed anterior spinal fusion as the ideal surgical intervention, and advocated doing it as soon as the diagnosis of spinal tuberculosis is made. The lesion may be curetted and drained at the time of operation, and in their experience patients have been able to resume normal function in four to six months. Then roentgenographic examination should be done every four to six months until evidence of healing is noted.

Summary

A case of disseminated bone tuberculosis has been presented, along with the pertinent clinical and roentgenographic findings. Multiple destructive lesions of bone warrant suspicion of primary tuberculous lesions elsewhere. Precise bacteriologic and histochemical studies are necessary to establish the diagnosis. Surgical intervention should be considered in selected cases.

REFERENCES

1. Alexander, G. H., and Mansuy, M. M.: Disseminated bone tuberculosis with case report, Radiology, 50:839-843, 1950.

2. Bosworth, D. M.: Treatment of tuberculosis of bone and joint, Bull. N. Y. Acad. Med., 35:167-177, 1959.

3. Bosworth, D. M., Pietra, A. D., and Rahilly, G.: Paraplegia resulting from tuberculosis of the spine, J. Bone and Joint Surg., 35-A:735-740, 1953.

4. Ellis, F. A.: Jungling's "osteitis tuberculosa multiplex cystoides" is not cystic tuberculous osteitis, Acta Med. Scand., 104:221-224, 1940.

5. Hodgson, A. R., and Stock, F. E.: Anterior spine fusion for the treatment of tuberculosis of the spine, J. Bone and Joint Surg., 42-A:295-310, 1960.

6. Hunt, D. D.: Problems in diagnosis osteo-articular tuberculosis, J.A.M.A., 190:95-98, 1964.

7. Jacobs, P.: Osteo-articular tuberculosis in colored immigrants: a radiological study, Clin. Rad., 19:59-69, 1964.

8. Kelley, W. H., and Sailer, S.: Disseminated tuberculosis of the skeleton, Am. Rev. Tuberc., 42:691-696, 1940.

9. Komins, C.: Multiple cystic tuberculosis: a review and a revised nomenclature, Brit. J. Rad., 25:1-8, 1952.

10. Lyford, J.: Disseminated tuberculosis of bone with multiple localizations in the skeleton: a report of two proved cases, J. Bone and Joint Surg., 25:453-460, 1943.

11. Marwah, V.: The changing pattern of osteo-articular tuberculosis, J. Indian Med. Assoc., 38:18-20, 1962.

12. McTammany, J. R., Moser, K. M., and Houk, V. N.: Disseminated bone tuberculosis, Amer. Rev. Resp. Dis., 87:889-895, 1963.

13. O'Malley, B. W., and Zeft, H. J.: Disseminated bone tuberculosis without pulmonary manifestations, Amer. J. Med., 38:932-936, 1965.

Myeloproliferative Disorder And Tuberculosis

IRVIN HERMAN, M.D., *Oakland*

ALTHOUGH the association of tuberculosis and hematologic disease has long been known, there is no supported understanding of their interrelationship. Clinically, the serologic abnormalities may be coexistent with or stimulated by the tuber-

From Highland-Alameda County Hospital.

Submitted 21 March 1966.

Reprint requests to: Respiratory Function Laboratory, Department of Medicine, Stanford Medical Center, 300 Pasteur Drive, Palo Alto, California 94304 (Dr. Herman).